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CONSERVATION OF BODY CALCIUM BY INCREASED DIETARY INTAKE OF POTASSIUM: A POTENTIAL MEASURE TO REDUCE THE OSTEOPOROSIS PROCESS DURING PROLONGED EXPOSURE TO MICROGRAVITY

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ABSTRACT

During the 1988 NASA Summer Faculty Fellowship Program, I proposed that the loss of skeletal calcium upon prolonged exposure to microgravity could be explained, in part, by a renal maladjustment characterized by an increased urinary excretion of calcium. We theorized that because the conservation of body fluids and electrolytes depends upon the energy of adenosine triphosphate and enzymes that control the use of its energy for renal ion transport, an induction of renal sodium and potassium-dependent adenosine triphosphatase (Na + K ATPase) by oral loading with potassium would increase the reabsorption of sodium directly and that of calcium indirectly, leading to improved hydration and to reduced calcium loss.

Preliminary studies showed the following. Rats drinking water containing 0.2 M potassium chloride for six to 13 days excreted in urine 22 μEq of calcium and 135 μEq of sodium per 100 grams of body weight per day. The corresponding values for control rats drinking tap water were 43 μEq and 269 μEq respectively. Renal Na + K ATPase activity in potassium loaded rats was higher than in controls. Thus, oral potassium loading resulted in increased Na + K ATPase activity and diminished urinary excretion of calcium and of sodium as predicted by our hypothesis.

An extension of these studies to humans has the potential of resulting in development of harmless, non-invasive, drug-free, convenient measures to reduce bone loss and other electrolyte and fluid problems in space travelers exposed to prolonged periods of microgravity.

INTRODUCTION

During Skylab flights, astronauts experienced an increased excretion of body calcium in urine (1). Last year, we proposed that the loss of calcium could be attributed to the reduced renal tubular reabsorption of the mineral (2). This resulted in urinary excretion of 0.29 gm of calcium per day during flight, up from 0.16 gm per day control rate. The net total calcium loss attributable to the kidney during the Skylab flights of 60 to 85 days equaled 7.8 gm to 11.05 gm respectively. The crewmen had an adequate average dietary intake of 0.73 gm calcium per day but went into negative calcium balance because fecal calcium excretion also increased (1,3). The calcium-wasting by the kidney is further demonstrated by the lack of renal conservation of calcium in the face of the increased fecal calcium losses.

To place the magnitude of the calcium loss in perspective, it is essential to realize that all extracellular body fluids contain only about 1 gm of calcium, cells contain 5 gm, and bone contains a total of 1,200 gm (4). Thus, any sizeable calcium loss, like that which occurred during the Skylab flights, must come eventually from bone. Calcium homeostasis involves continuous mineral turnover in bone, absorption from food and reabsorption by the kidney. Overall calcium metabolism is primarily set to maintain a constant calcium concentration in extracellular fluid, even at the expense of bone density. Absorption from the gut is controlled by vitamin D, bone resorption and renal reabsorption are promoted by parathyroid hormone and inhibited by calcitonin (4,5).

Based on the above considerations, options for prevention of calcium loss are: 1) increase intake and/or decrease losses of calcium from the gut; 2) decrease calcium loss from bone; and 3) decrease calcium loss from the kidney. Relative to option 1, stable and adequate calcium intake during Skylab flights did not prevent negative calcium balance (1,3). In fact, there was an increased amount of calcium lost in feces (3). Enhancement of calcium absorption from food deserves further study.

Decreased egress of calcium from bone appears to be under most intensive investigation at present as a solution to bone demineralization during space flight. In our opinion, producing a halt to bone resorption without increased absorption from the gut and reduced loss via the kidneys would lead to a reduced intracellular and extracellular calcium concentration. Since calcium is required for muscular contraction and nerve conduction, inadequate calcium levels may lead to increased weakness and atrophy, already a problem during space flight (6). Diminished supply of calcium to the heart could lead to impairment of cardiac output and to irregularities of heart rhythm (arrhythmias) that could result in sudden death.

Relative to the third option, reversal of the acquired defect in tubular reabsorption of calcium would be a desirable solution to the excessive calcium loss during space flight. Because renal calcium reabsorption is in part dependent upon the transport of sodium, we propose that an induction of renal sodium and potassium-dependent adenosinetriphosphatase (Na + K ATPase), an enzyme system that allows the use of adenosine triphosphate (ATP) for ion transport (7), would improve tubular reabsorption of sodium directly and that of calcium secondarily. In addition to calcium conservation, this maneuver would improve reabsorption of sodium, chloride and water, all of which are also excessively lost during space flight. Practical methods for induction of renal Na + K ATPase deserve further investigation in an attempt to prevent osteoporosis and fluid and electrolyte loss associated with space travel. The magnitude of renal-related calcium losses, coupled with the fact that Skylab astronauts had adequate calcium intake and excessive fecal calcium losses, make it wise to consider ways in which renal losses of calcium can be curtailed.

METHODS

Chronic dietary administration of potassium salts appears to be a harmless method of inducing renal Na + K ATPase activity (8,9). After several trials, we devised the following protocol to study the effects of oral potassium loading on urinary calcium excretion in rats. Sprague-Dawley female

rats, 200 - 250 grams, were divided into four groups. Each group of two rats was kept in a separate holding cage. Food, Purina's Formulate 5008, was offered ad libitum. Drinking fluids were as follows: Group 1: 0.2 M potassium chloride; group 2: 0.3 M potassium chloride; group 3: 0.2 M sodium chloride; group 4: tap water. After six days of this regimen, one rat from each group was placed in an individual Nalge Metabolism Cage (Fisher Scientific) for a 24 hour urine collection. No food or fluid was given on that day. Urinary calcium, potassium and sodium were measured by atomic absorption spectrophotometry. The experiment was repeated seven days later with the remaining rats. Promptly after each experiment, kidneys were removed under pentobarbital (60 mg/kg i.p.) anesthesia for determination of Na + K ATPase activity using methods described previously (10). Briefly, whole kidney tissue homogenates were prepared 1:10 in a sucrose solution containing Tris (hydroxymethyl)-aminomethane, disodium edtate, and sodium deoxycholate. Enzyme activity was measured by the rate of release of inorganic phosphate (Pi) from exogenous ATP during 20 minutes of incubation at 37 degrees C. The incubation mixture contained the enzyme source (subdiluted kidney homogenate, 100 mM NaCl, 3 mM MgCl2, 3 mM ATP, and 40 mM HEPES (N-2-hydroxyethylpiperazine-N'-2-ethanesulphonic acid) buffer at pH 7.4. Enzyme activity inhibited by 2 x 10^{-3} Mouabain represented Na + K ATPase activity.

RESULTS

These preliminary results (Table) are based on data from two rats per group. The outstanding observation is that six and 13 days of potassium loading via drinking water resulted in about one half as much urinary calcium excretion than that of control animals loaded with sodium or tap water. Potassium-induced calcium conservation was accompanied by selectively higher renal Na + K ATPase specific activity, ie., sensitive to ouabain, than that found in control groups. Ouabain-insensitive ATPase specific activity was essentially the same in all groups.

DISCUSSION

There is sufficient knowledge of renal handling of calcium (4) to formulate rational experiments aimed at reducing urinary excretion of calcium when and if indicated. Briefly, the protein-unbound portion of blood calcium is filtered through the glomeruli. Normally, over 98% of this calcium is reabsorbed by the renal tubules and the remaining fraction is excreted in the urine. To some degree, the tubular reabsorption of calcium is dependent upon the reabsorption of sodium which, to a large extent, utilizes the ubiquitous Na and K pump driven by the Na + K ATPase system. Accordingly, inhibition of renal Na + K ATPase by digitalis glycosides results not only in natriuresis but also in increased excretion of calcium (7). We have modified the method of Epstein's group (8,9) to induce renal Na + K ATPase activity by an increased dietary offering of potassium to rats. Predictably, our experiments resulted in renal conservation of sodium and calcium.

The same phenomena are probably operational in humans. Pak's data (11) in patients treated for months with potassium citrate for nephrolithiasis suggest renal conservation of calcium, but the study was not specifically designed to bring out this feature.

In Skylab astronauts, urinary potassium excretion, and thus dietary intake, was on the order of three grams (1) or even 1.5 grams (3). These amounts correspond to the average dietary potassium intake of the general population in Western countries.

Louis Tobian, a pioneer in investigating the link between low potassium intake and high blood pressure diseases, suggested that people increase their average daily intake of potassium to six grams (12). We suggest that a similar regimen would be reflected in renal conservation of calcium as well.

Renal calcium conservation may be relevant to the prevention of osteoporosis. There is a growing awareness that osteoporosis has a dietary component whereby high salt intake contributes to the loss of calcium (13, 14). We would like to expand upon these emerging views by proposing that osteoporosis is exacerbated by low dietary intake of potassium.

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TABLE

Effects of potassium chloride or sodium chloride added to drinking water on urinary calcium, potassium and sodium excretion and renal Na + K ATPase activity in rats.

GROUP 1		GROUP 2		GROUP 3		GROUP 4		GROUP 1	GROUP 2	GROUP 3	GROUP 4
Salts added to drinking water, M.											
KCl 0.2		KCl 0.3		NaCl 0.2		0		KCl 0.2	KCl 0.3	NaCl 0.2	0
Rat #1	Rat #2	Rat #1	Rat #2	Rat #1	Rat #2	Rat #1	Rat #2	Mean, Rats #1 & #2			
(Rats #1 treated for 6 days, Rats #2 treated for 13 days)											
Mean daily fluid consumption, ml/100 g body weight											
15.9	13.7	24.0	15.4	29.3	27.0	11.1	9.7	14.8	19.7	28.2	10.4
No food or fluids on day of 24 hour urine collection (day 7 for Rats #1, day 14 for Rats #2)											
Urine flow, ml/100 g/24 h											
1.7	1.6	3.0	2.0	4.1	3.0	4.5	2.5	1.7	2.5	3.6	3.5
Calcium, µEq/100 g/24 h											
22	22	30	18	44	34	50	36	22	24	39	43
Potassium, µEq/100 g/24 h											
458	425	792	556	420	422	456	416	442	674	421	436
Sodium, µEq/100 g/24 h											
137	133	179	144	416	382	343	194	135	162	399	262
Na + K ATPase Activity in Whole Kidney Homogenates µmol Pi/mg protein/hr								10	12	7	9
Ouabain-insensitive ATPase activity µmol Pi/mg protein/hr								14	14	13	14